

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 10 August 2000 (10.08.00)	
International application No. PCT/JP99/06412	Applicant's or agent's file reference 661607
International filing date (day/month/year) 17 November 1999 (17.11.99)	Priority date (day/month/year) 17 November 1998 (17.11.98)
Applicant KATO, Seishi et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

05 June 2000 (05.06.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>Alejandro HENNING</p> <p>Telephone No.: (41-22) 338.83.38</p>
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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 661607	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/JP 99/06412	International filing date (day/month/year) 17/11/1999	(Earliest) Priority Date (day/month/year) 17/11/1998
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 10 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☒ Unity of invention is lacking (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 99/06412

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1 - 6 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:21) and subject-matter relating thereto.

2. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:22) and subject-matter relating thereto.

3. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:23) and subject-matter relating thereto.

4. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:24) and subject-matter relating thereto.

5. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:25) and subject-matter relating thereto.

6. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:26) and subject-matter relating thereto.

7. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:27) and subject-matter relating thereto.

8. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:28) and subject-matter relating thereto.

9. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:29) and subject-matter relating thereto.

10. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:30 and subject-matter relating thereto.

11. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:51) and subject-matter relating thereto.

12. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:52) and subject-matter relating thereto.

13. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:53) and subject-matter relating thereto.

14. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:54) and subject-matter relating thereto.

15. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:55) and subject-matter relating thereto.

16. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:56) and subject-matter relating thereto.

17. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:57) and subject-matter relating thereto.

18. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:58) and subject-matter relating thereto.

19. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:59) and subject-matter relating thereto.

20. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:60) and subject-matter relating thereto.

21. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:81) and subject-matter relating thereto.

22. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:82) and subject-matter relating thereto.

23. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:83) and subject-matter relating thereto.

24. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:84) and subject-matter relating thereto.

25. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:85) and subject-matter relating thereto.

26. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:86) and subject-matter relating thereto.

27. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:87) and subject-matter relating thereto.

28. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

(SEQ ID NO:88) and subject-matter relating thereto.

29. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:89) and subject-matter relating thereto.

30. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:90) and subject-matter relating thereto.

31. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:111) and subject-matter relating thereto.

32. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:112) and subject-matter relating thereto.

33. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:113) and subject-matter relating thereto.

34. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:114) and subject-matter relating thereto.

35. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:115) and subject-matter relating thereto.

36. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:116) and subject-matter relating thereto.

37. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:117) and subject-matter relating thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

38. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:118) and subject-matter relating thereto.

39. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:119) and subject-matter relating thereto.

40. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:120) and subject-matter relating thereto.

41. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:141) and subject-matter relating thereto.

42. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:142) and subject-matter relating thereto.

43. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:143) and subject-matter relating thereto.

44. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:144) and subject-matter relating thereto.

45. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:145) and subject-matter relating thereto.

46. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:146) and subject-matter relating thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

47. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:147) and subject-matter relating thereto.

48. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:148) and subject-matter relating thereto.

49. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:149) and subject-matter relating thereto.

50. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:150) and subject-matter relating thereto.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/JP 99/06412

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07K14/705 C12N15/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAGARA ET AL.: "Molecular cloning, differential expression, and chromosomal localization of human Frizzled-1, Frizzled-2, and Frizzled-7" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 252, no. 1, 9 November 1998 (1998-11-09), pages 117-122, XP002132622 abstract; figures 1-4	1-6
Y	WO 98 21328 A (KATO SEISHI ;PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998 (1998-05-22) page 7, paragraph 2 -page 8, paragraph 1 --- -/ --	1-6

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

9 March 2000

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Sprinks, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 99/06412

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>BUCHER ET AL: "A flexible motif search technique based on generalized profiles" COMPUTERS AND CHEMISTRY,GB,PERGAMON PRESS, OXFORD, vol. 20, no. 1, 1996, pages 3-23, XP002107535 ISSN: 0097-8485 the whole document</p> <p>---</p>	1-6
A	<p>D'ANDREA ET AL: "Molecular Cloning of NKB1. A Natural Killer Cell Receptor for HLA-B Allotypes" JOURNAL OF IMMUNOLOGY,US,THE WILLIAMS AND WILKINS CO. BALTIMORE, vol. 155, no. 5, 1 September 1995 (1995-09-01), pages 2306-2310-2310, XP002111500 ISSN: 0022-1767 the whole document</p> <p>---</p>	1-6
A	<p>GILLEN C M ET AL: "Molecular cloning and functional expression of the K-C1 cotransporter from rabbit, rat, and human" JOURNAL OF BIOLOGICAL CHEMISTRY,US,AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, vol. 271, no. 27, 5 July 1996 (1996-07-05), pages 16237-16244-16244, XP002119528 ISSN: 0021-9258 the whole document</p> <p>---</p>	1-6
A	<p>KYTE J ET AL: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY,GB,LONDON, vol. 157, no. 1, 5 May 1982 (1982-05-05), pages 105-132, XP000609692 ISSN: 0022-2836 the whole document</p> <p>-----</p>	1-6

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 99/06412

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9821328 A	22-05-1998	AU 4885297 A EP 0941320 A	03-06-1998 15-09-1999

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 661607		FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP99/06412	International filing date (day/month/year) 17/11/1999	Priority date (day/month/year) 17/11/1998		
International Patent Classification (IPC) or national classification and IPC C07K14/705				
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al.				

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 05/06/2000	Date of completion of this report 12.03.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Sprinks, M Telephone No. +49 89 2399 8706 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP99/06412

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).:*)

Description, pages:

1-124 as originally filed

Claims, No.:

1-6 as originally filed

Drawings, sheets:

1/50-50/50 as originally filed

Sequence listing part of the description, pages:

1-233, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/JP99/06412

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-6 (partially).

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1-6 (partially).

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/JP99/06412

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
- ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-6 (partially).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-6
	No:	Claims
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-6
Industrial applicability (IA)	Yes:	Claims 1-6
	No:	Claims

2. Citations and explanations
see separate sheet

The following documents (D) are mentioned for the first time in this opinion/report; the numbering will be adhered to in the rest of the procedure:

D1: Biochemical And Biophysical Research Communications (09-11-1998),
252(1), 117-122

D2: WO-A-9821328

D3: Computers And Chemistry,gb,pergamon Press, Oxford (1996), 20(1), 3-23

IV) Unity

The International Searching Authority made an objection concerning lack of unity of invention for the originally filed application, identifying 50 different inventions. However, since the applicant declined to pay additional taxes, both international search and substantive examination have been limited to the first invention identified in **claims 1-6**, i.e. to a cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:21) and subject-matter relating thereto.

V) Reasoned statement

Inventive Step

- 1) The present application does not satisfy the criterion set forth in **Article 33 (3) PCT** because the subject-matter of **claims 1-6** does not involve an inventive step (**Rule 65.1 and 65.2 PCT**).
- 2) The cDNA encoding the protein referred to in claim 1 differs from that of D1 (human Frizzled-1) only at one base in the coding sequence, resulting in a single conservative amino acid substitution (Ala to Thr).

Consequently, absent any surprising technical effect associated with such a substitution, both the cDNA and protein claimed in the present application must be considered to be the result of arbitrary selection from obvious alternatives and therefore non-inventive (as must the expression vector and host cell associated therewith).

- 3) However, even in the absence of D1, the claimed subject-matter could still not be considered inventive for the following reasons:

Although the application discloses a nucleotide sequence corresponding to a cDNA clone isolated from a human cDNA library and the "best guess" open reading frame (ORF) identifiable with it, it provides no tangible evidence of the expression of the putatively encoded polypeptide or its biological role. To simply state that the isolated cDNA is likely to encode a polypeptide which may have certain properties is not sufficient to irrefutably establish its function. The extensive list of possible functions given in the description confuses this situation still further, making it clear that at the date of filing the present application, the applicants were not aware of what the claimed polypeptide actually was.

Consequently, the invention of the present application is merely considered to be the provision of a transcribed sequence ("a compound") with no known technically useful property. In this case any prior art compound, regardless of its technical properties, is equally suitable as the starting point for making structural modifications and may be considered to represent "the closest prior art".

Starting from this point, the only technical problem which may be derived is how to provide a different compound.

Without the concomitant need to provide any particular technical effect, the skilled person would have the choice of an infinite number of equally obvious possible solutions. An arbitrary selection from this list cannot involve an inventive step because, in order to be patentable, a selection must be justified by a technical purpose, i.e. by a hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all the other possibilities.

Thus, for nucleotide and peptide sequences whose function and, in the latter case, existence is based purely upon surmise, inventive step cannot be acknowledged.

Furthermore, if an invention should provide a solution to a problem with reference

to the background art (**Rule 5.1 (a) (iii) PCT**), the "invention" of the present application is insufficiently disclosed (**Article 5 PCT**) and unclear (**Article 6 PCT**), since it is left to the reader to perform the invention and determine what problem, if any, the isolated nucleotide or hypothetical polypeptide sequences actually solve.

In any event, taking D2 as the closest prior art, a skilled person looking for further proteins with hydrophobic domains would simply use the conserved sequence structures disclosed in said document to search an appropriate sequence database using routine sequence and motif search techniques - see D3. He would thus extract the desired sequence information from the database in an obvious manner without performing a single experiment (but also without confirming any specific function of the "fished" polypeptide or that it could be produced without undue burden or the application of inventive skill).

091850231

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
25 May 2000 (25.05.2000)

PCT

(10) International Publication Number
WO 00/29448 A3

(51) International Patent Classification⁶: **C07K 14/705**,
C12N 15/12

Nishiikuta, Tama-ku, Kawasaki-shi, Kanagawa 214-0037 (JP).

(21) International Application Number: PCT/JP99/06412

(74) Agents: **AOYAMA, Tamotsu** et al.: Aoyama & Partners, IMP Building, 3-7, Shiromi 1-chome, Chuo-ku, Osaka-shi, Osaka 540-0001 (JP).

(22) International Filing Date:
17 November 1999 (17.11.1999)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/326255 17 November 1998 (17.11.1998) JP
10/364315 22 December 1998 (22.12.1998) JP
11/69811 16 March 1999 (16.03.1999) JP
11/119299 27 April 1999 (27.04.1999) JP
11/138169 19 May 1999 (19.05.1999) JP

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) Abstract: The present invention provides human proteins having hydrophobic domains, DNAs encoding these proteins, and expression vectors for these DNAs as well as eukaryotic cells expressing these DNAs.

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/JP 99/06412

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/705 C12N15/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAGARA ET AL.: "Molecular cloning, differential expression, and chromosomal localization of human Frizzled-1, Frizzled-2, and Frizzled-7" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 252, no. 1, 9 November 1998 (1998-11-09), pages 117-122, XP002132622 abstract; figures 1-4	1-6
Y	WO 98 21328 A (KATO SEISHI ;PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998 (1998-05-22) page 7, paragraph 2 -page 8, paragraph 1 -/-	1-6

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

9 March 2000

Date of making of the international search report

23.06.00

Name and mailing address of the ISA

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Sprinks, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 99/06412

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>BUCHER ET AL: "A flexible motif search technique based on generalized profiles" COMPUTERS AND CHEMISTRY,GB,PERGAMON PRESS, OXFORD, vol. 20, no. 1, 1996, pages 3-23, XP002107535 ISSN: 0097-8485 the whole document</p> <p>---</p>	1-6
A	<p>D'ANDREA ET AL: "Molecular Cloning of NKB1. A Natural Killer Cell Receptor for HLA-B Allotypes" JOURNAL OF IMMUNOLOGY,US,THE WILLIAMS AND WILKINS CO. BALTIMORE, vol. 155, no. 5, 1 September 1995 (1995-09-01), pages 2306-2310-2310, XP002111500 ISSN: 0022-1767 the whole document</p> <p>---</p>	1-6
A	<p>GILLEN C M ET AL: "Molecular cloning and functional expression of the K-C1 cotransporter from rabbit, rat, and human" JOURNAL OF BIOLOGICAL CHEMISTRY,US,AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, vol. 271, no. 27, 5 July 1996 (1996-07-05), pages 16237-16244-16244, XP002119528 ISSN: 0021-9258 the whole document</p> <p>---</p>	1-6
A	<p>KYTE J ET AL: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY,GB,LONDON, vol. 157, no. 1, 5 May 1982 (1982-05-05), pages 105-132, XP000609692 ISSN: 0022-2836 the whole document</p> <p>-----</p>	1-6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 99/06412

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1 - 6 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:21) and subject-matter relating thereto.

2. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:22) and subject-matter relating thereto.

3. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:23) and subject-matter relating thereto.

4. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:24) and subject-matter relating thereto.

5. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:25) and subject-matter relating thereto.

6. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:26) and subject-matter relating thereto.

7. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:27) and subject-matter relating thereto.

8. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:28) and subject-matter relating thereto.

9. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:29) and subject-matter relating thereto.

10. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:30 and subject-matter relating thereto.

11. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:51) and subject-matter relating thereto.

12. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:52) and subject-matter relating thereto.

13. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:53) and subject-matter relating thereto.

14. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:54) and subject-matter relating thereto.

15. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:55) and subject-matter relating thereto.

16. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:56) and subject-matter relating thereto.

17. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:57) and subject-matter relating thereto.

18. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:58) and subject-matter relating thereto.

19. Claims: 1-6 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:59) and subject-matter relating thereto.

20. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:60) and subject-matter relating thereto.

21. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:81) and subject-matter relating thereto.

22. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:82) and subject-matter relating thereto.

23. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:83) and subject-matter relating thereto.

24. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:84) and subject-matter relating thereto.

25. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:85) and subject-matter relating thereto.

26. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:86) and subject-matter relating thereto.

27. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:87) and subject-matter relating thereto.

28. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

(SEQ ID NO:88) and subject-matter relating thereto.

29. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:89) and subject-matter relating thereto.

30. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:90) and subject-matter relating thereto.

31. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:111) and subject-matter relating thereto.

32. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:112) and subject-matter relating thereto.

33. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:113) and subject-matter relating thereto.

34. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:114) and subject-matter relating thereto.

35. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:115) and subject-matter relating thereto.

36. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:116) and subject-matter relating thereto.

37. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains
(SEQ ID NO:117) and subject-matter relating thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

38. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:118) and subject-matter relating thereto.

39. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:119) and subject-matter relating thereto.

40. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:120) and subject-matter relating thereto.

41. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:141) and subject-matter relating thereto.

42. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:142) and subject-matter relating thereto.

43. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:143) and subject-matter relating thereto.

44. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:144) and subject-matter relating thereto.

45. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:145) and subject-matter relating thereto.

46. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:146) and subject-matter relating thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

47. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:147) and subject-matter relating thereto.

48. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:148) and subject-matter relating thereto.

49. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:149) and subject-matter relating thereto.

50. Claims: 1-6 partially

A cDNA encoding a human protein having hydrophobic domains (SEQ ID NO:150) and subject-matter relating thereto.

information on patent family members

PCT/JP 99/06412

Form PCT/ISA/210 (patent family annex) (July 1992)